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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application of: Spear *et al.*	Confirmation No.: 3399
Application No.: 09/924,231	Group Art Unit: 1648
Filed: August 8, 2001	Examiner: Wortman, D.
For: PHARMACEUTICAL COMPOSITIONS COMPRISING HERPES VIRUS ENTRY RECEPTOR PROTEIN	Attorney Docket No.: 7853-239

RESPONSE TO OFFICE ACTION

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

In response to the Office Action dated March 5, 2002, please consider the remarks below intended. Applicants submit herewith (1) a Petition for Extension of Time for two months from June 5, 2002, up to and including August 5, 2002; (2) Exhibit A, a copy of the pending claims; (3) Exhibit B, a Declaration under 37 C.F.R. § 1.132 by Dr. Abbie Celniker[1] (with Exhibits 1-9); (4) an Information Disclosure Statement; and (5) a List of References Cited.

REMARKS

Claims 1-5 are pending in this application. The language of the Office Action of March 5, 2002 indicates that the Examiner acknowledges that claims 1-5 are pending in the instant application. However, the Office Action Summary sheet indicate that only claims 1-4 are pending. Applicants respectfully request correction of this error in future communications from the Patent Office.

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[1] The Declaration is being filed unexecuted; an executed counterpart will be submitted at the earliest opportunity.

THE REJECTIONS UNDER 35 U.S.C. § 112, FIRST PARAGRAPH, SHOULD BE WITHDRAWN

Claims 1-5 are directed to pharmaceutical compositions comprising a recombinant soluble human HVEM polypeptide. While acknowledging that the specification teaches how to make the claimed pharmaceutical compositions, the Examiner contends that the specification fails to provide guidance that would enable the skilled artisan on how to use the compositions, because the "the specification does not disclose that there is any beneficial effect as a result of treating with the claimed composition." The Examiner further states that, although "it is apparent from the disclosure that the pharmaceutical use contemplated is that of a treatment or preventative for human herpesvirus infections," the specification indicates that "merely preventing the virus from binding to cell surface HVEM would be insufficient to prevent entry of the virus into human cells *in vivo*." This rejection should be withdrawn for the reasons presented below.

Applicants provide evidence that corroborates the disclosure in the specification with regard to the utility and enablement of the use of pharmaceutical compositions comprising soluble HVEM as claimed. This evidence is presented by way of a Declaration under 37 C.F.R. § 1.132 of Dr. Abbie Celniker (Rule 132 Declaration) and the attached Exhibits 2-9, attached hereto as Exhibit A.

As of the effective filing date of the instant specification, one of skill in the art would clearly appreciate, upon reading the specification, that a pharmaceutical composition comprising a soluble HVEM could be used to block herpes virus from infecting a cell and/or to inactivate herpes virus replication. It was well established, prior to the filing of the instant application, that (i) soluble TNF receptors, of which HVEM is a family member, sequester the receptors' ligands and in doing so inhibit the ligands' biological function, and that (ii) soluble viral entry receptors block virus entry into a target cell and are useful in treating or preventing viral infection (see 132 Declaration at paragraphs 6-11).

Although a number of cellular herpes virus receptors have been identified since the effective filing date of the present application, strains of both wild type HSV1 and HSV2 are capable of binding to and entering mammalian cells through HVEM. *See* 132 Declaration at paragraph 13. HSV1 and HSV2 bind to HVEM through glycoprotein D ("gD"). *See* 132 Declaration at paragraph 13. The region of gD which binds to HVEM

mediates the binding of gD to other cellular receptors. *See* 132 Declaration at paragraph 14. Thus, administration of soluble HVEM to an individual will prevent gD from binding to cellular receptors other than HVEM, and therefore will prevent infection of cells by strains of herpes virus that are capable of binding to HVEM. *See* 132 Declaration at paragraphs 16 and 17. Therefore, the expectations of one of skill in the art at the time of filing the present application are borne out by post-filing date evidence.

Applicants further remind the Examiner that Section 112 does not require that optimal efficacy be provided by the invention, merely that some efficacy be provided. This requirement is clearly met by the instant application and the data discussed in the Rule 132 Declaration, which concludes that administration of pharmaceutical compositions comprising soluble HVEM would "be useful in achieving clinically beneficial results in the treatment or prevention of infections by wild type HSV1 and HSV2." The Examiner's attention is also directed to MPEP 2164.07, which states that:

> ... the character and amount of evidence needed to support an asserted utility will vary depending on what is claimed (*Ex parte Ferguson*, 117 USPQ 229, 231 (Bd. App. 1957)), and whether the asserted utility appears to contravene established scientific principles and beliefs. *In re Gazave*, 379 F.2d 973, 978, 154 USPQ 92, 96 (CCPA 1967); *In re Chilowsky*, 229 F.2d 457, 462, 108 USPQ 321, 325 (CCPA 1956). Furthermore, the applicant does not have to provide evidence sufficient to establish that an asserted utility is true "beyond a reasonable doubt." *In re Irons*, 340 F.2d 974, 978, 144 USPQ 351, 354 (CCPA 1965). Instead, evidence will be sufficient if, considered as a whole, it leads a person of ordinary skill in the art to conclude that the asserted utility is more likely than not true.

See also MPEP § 2164.01(c) (stating that "when a compound or composition claim is not limited by a recited use, any enabled use that would reasonably correlate with the entire scope of that claim is sufficient to preclude a rejection for nonenablement based on how to use").

Given the foregoing standard for enablement, and for the reasons discussed above and in the Rule 132 Declaration, one of skill in the art would recognize how to use pharmaceutical compositions comprising HVEM polypeptides, for example soluble HVEM. In particular, one of skill in the art would recognize that an exogenous HVEM, for example an HVEM protein administered to a patient in the form of a pharmaceutical composition, would bind to herpes virus particles of strains 1 and 2, thereby sequestering the virus and

preventing it from binding the membrane bound cellular receptor and being taken up by cells that express a cellular receptor for the herpes virus. This inhibition of viral entry is analogous to gD interference, whereby infection of a cell with herpes virus renders the cell resistant to subsequent viral infection, even if the subsequent infection is by another strain of herpes virus, because the interaction between gD expressed by the cell and a cellular receptor such as HVEM sequesters the receptor from mediating the *de novo* uptake of viral particles. One of skill in the art would also recognize that because of its aforementioned properties, a pharmaceutical composition comprising an HVEM protein, for example a soluble HVEM protein, would be useful in treating or preventing herpes virus infection, at least where the infection is caused by a wild type strain of HSV1 or HSV2.

In view of the remarks above, Applicants submit that the specification as filed provides sufficient support under Section 112 for the claimed pharmaceutical compositions. Applicants respectfully assert that the rejection is improper and, as such, Applicants request that the rejection of claims 1-5 under 35 U.S.C. § 112, first paragraph, be withdrawn.

DOUBLE PATENTING REJECTION

Claims 1-5 are rejected under the judicially created doctrine of obviousness-type double patenting over claims 1-4 of U.S. Patent No. 6,303,336.

While not admitting that the claims of the above-identified patent application are not patentably distinct from the claims of U.S. Patent No. 6,303,336, Attorneys for Applicants hereby state that a Terminal Disclaimer under 37 C.F.R. § 1.321(b) will be supplied to the Patent and Trademark Office when the application is indicated to be in form for grant but for a Terminal Disclaimer. Applicants request that this rejection be held in abeyance until allowable subject matter is indicated.

CONCLUSION

Applicants respectfully request consideration of the foregoing remarks. Applicants believe the claims to be in condition for allowance.

Respectfully submitted,

Date: August 5, 2002

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By: Muna Abu-Shaar

Muna Abu-Shaar
Limited Recognition Under 37 C.F.R. § 10.9(b)
Copy of Certificate Enclosed

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Enclosure